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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/753,289	01/05/2004	Steven M. Watkins	475512000100	1703

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EXAMINER

NEGIN, RUSSELL SCOTT

ART UNIT	PAPER NUMBER
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1631

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12/03/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/753,289	Applicant(s) WATKINS, STEVEN M.	
	Examiner RUSSELL S. NEGIN	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-17 and 56-58 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-17 and 56-58 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Comments

Applicants' amendments and request for reconsideration in the communication filed on 25 August 2008 are acknowledged and the amendments are entered.

Claims 2-17 and 56-58 are pending and examined in the instant Office action.

Withdrawn Rejections

Applicant's arguments, see page 7 of the Remarks filed 25 August 2008, with respect to the rejection(s) of claim(s) 2-17 and 56-59 under 35 U.S.C. 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Dionisi et al. [Lipids, volume 34, 1999, pages 1107-1115] in view of Ruan et al. [Journal of Dairy Science, 1998, volume 80, pages 9-15].

Claim Rejections - 35 USC § 101

The following rejection is newly applied:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2-17 and 56-58 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The method claims of the instant application (instant claims 2-17 and 56-58) recite a series of steps without a physical transformation. Further, the claims fail to recite a tie to a machine. It is noted that while the result of the calculation is displayed as a heat map, this final step is an insignificant post-solution activity and does not constitute a significant tie to another category of invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The following rejections are newly applied:

Rejection #1 under 35 U.S.C. 103(a):

Claims 2-3, 5-7, 15-16, and 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dionisi et al. [Lipids, volume 34, 1999, pages 1107-1115] in view of Ruan et al. [Journal of Dairy Science, volume 81, 1998, pages 9-15].

Claim 2 is drawn to a method for presenting analysis of quantitative lipid metabolite profiles, comprising:

--designating (a) a first quantitative lipid metabolite profile from a first biological sample and (b) a second quantitative lipid metabolite profile from a second biological sample that is different from the first biological sample:

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--identifying differences or similarities in a plurality of individual lipid metabolites between the first and second quantitative lipid metabolite profiles;
--and displaying the identified differences or similarities on a heat map.

The article of Dionisi et al. studies the stability of cyclopropane and conjugated linoleic acids during fatty acid quantification in lactic acid bacteria.

Specifically, Table 3 on page 1114 of Dionisi et al. tabulates the fatty acid composition of five lyophilized bacterial samples. As Table 3 of Dionisi et al. the fatty acid profiles of the different profiles are different; differences between the fatty acid profiles are quantified and identified by comparisons of the values for each sample in Table 3 of Dionisi et al.

However, Table 3 of Dionisi et al. is not an actual heat map.

The article of Ruan et al. studies MRI imaging techniques applied to two distinct experiments: water/oil emulsions and cheese block analyses.

The term "heat map" is not explicitly recited in Ruan et al.

On page 37, lines 17-19, applicant defines heat map as:

In a heat map display, quantitative metabolite data from a test sample is compared to quantitative metabolite data from a base line or standard sample (a control) and the increase or decrease in each metabolite is indicated on the display, usually in a readily recognizable fashion.

It is inherent that the illustration in Figure 5 of Ruan et al. is a heat map because it is a two dimensional map of multiple lipid profiles marked by shades of colors.

Claim 3 is further limiting with the additional limitation of the quantitative lipid metabolite profiles comprising quantitative measures of at least two individual lipids

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wherein the quantified measurements are obtained using an internal standard for at least one of the lipids.

Table 3 of Dionisi et al. quantifies the amount of individual lipids for a plurality of individual lipids. Figure 1 on page 1110 of Dionisi et al. illustrates a chromatogram comprising a subset of the lipids in Table 3 wherein the internal standard is tetradecene.

Claim 5 is further limiting with the additional limitation that the quantitative lipid metabolite profiles each comprise a quantified measurement of individual lipids in a lipid class.

Claim 6 is further limiting wherein the quantified measurement of the individual lipids in the lipid class is obtained using an internal standard for the lipid class.

Table 3 of Dionisi et al. lists a plurality of lipids in a lipid class (i.e. there are a plurality of unsaturated lipids).

Figure 1 on page 1110 of Dionisi et al. illustrates a chromatogram comprising a subset of the lipids in Table 3 wherein the internal standard is tetradecene.

Claim 7 is further limiting wherein the additional lipid comprises the fatty acid 18:0. Table 3 on page 1114 of Dionisi et al. lists 18:0 as a type of lipid.

Claims 15-16 are further limiting comprising separating and measuring using chromatography.

The procedure of chromatography is described in the first column on page 1109 of Dionisi et al. and the chromatogram is displayed in Figure 1 on page 1110 of Dionisi et al.

Claim 56 is further limiting wherein an increase or decrease in the individual lipid metabolite is indicated on the heat map by a color and the relevant amount of the increase or decrease is indicated by the intensity of the color.

Table 3 of Dionisi et al. illustrates a plurality of individual lipid metabolite profiles.

The “heat maps” in Figure 5 of Ruan et al. illustrate such a trend in colors with respect to lipid content.

Claim 57 is further limiting, further comprising generating a written report.

Table 3 of Dionisi et al. is a written report.

Claim 58 is further limiting wherein one of the quantitative lipid metabolite profiles is a control lipomic profile.

In this instance, the first fatty acid profile of the plurality of profiles in Dionisi et al. is considered a control lipomic profile.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to modify the lipomic profiles of Dionisi et al. by use of the display of the results as a heat map analysis of lipids in Ruan et al. because it is obvious to

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combine known elements in the prior art to yield a predictable result. In this instance, it would have been obvious to combine the heat maps of Ruan et al. with the lipomic profiles of Dionisi et al. to yield an alternative method of displaying the lipomic profiles within a sample. There would have been a reasonable expectation of success in combining Dionisi et al. with Ruan et al. because both studies are applied to the analogous problem of understanding lipid profiles in biological samples.

Response to Arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection. It is noted that while the reference of Ruan et al. is reiterated from the previous Office action, its role in the instant rejection is limited to displaying the results of Dionisi et al. as a heat map.

The following rejection is newly applied:

Rejection #2 under 35 U.S.C. 103(a):

Claims 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dionisi et al, in view of Ruan et al. as applied to claims 2-3, 5-7, 15-16, and 56-58 above in further view of Watkins et al. [Journal of Lipid Research, volume 39, 1998, pages 1583-1588].

Claims 9 and 13 are further limiting with the additional limitation of requiring cardiolipins.

Dionisi et al. and Ruan et al. make obvious a comparative profile of lipid concentrations, as discussed above.

Dionisi et al. and Ruan et al. do not teach use of cardiolipins.

The study of Watkins et al., entitled, "Docosahexaxenoic acid accumulates in cardiolipin and enhances HT-29 cell oxidant production," states in the first sentence of the abstract, "The objective of this study was to investigate membrane fatty acids for their effects on mitochondrial function in live cells."

The top of column 2 of page 1583 details some of the specific lipid studied, as stated, "In mammals, CL acyl composition is unusually sensitive to diet, and in humans it is rich in the essential fatty acid linoleic acid (LA, 18:2 n-6)." (a cardiolipin)

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid composition study of Dionisi et al. and Ruan et al. by use of the cardiolipin study of Watkins et al., wherein the motivation would have been that while Dionisi et al. and Ruan et al. quantify lipids, Watkins et al. has the advantage of quantifying cardiolipins in mitochondria for the purpose of understanding oxidant production and aging (see abstract of Watkins et al.).

Response to arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

The following rejection is newly applied:

Rejection #3 under 35 U.S.C. 103(a):

Claims 4 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dionisi et al. in view of Ruan et al. in view of Watkins et al. as applied to claims 2-3, 5-7, 15-16, and 56-58 above in further view of Siguel [US Patent 5,075,101; IDS of 1/5/2004].

Claims 4 and 14 are further limiting, limiting the metabolites to **5,8,11-eicosatrienoic acid, 5,8,11,14,17-eicosapentaenoic acid, 5,8,11-eicosatrienoic acid, and 5,8,11,14,17-eicosapentaenoic acid.**

Dionisi et al., Ruan et al., and Watkins et al., make obvious the method of fatty acid analysis, as discussed above.

However, these three sources do not teach the specific molecules of the claims, including the above mentioned 5,8,11-eicosatrienoic acid (Mead acid).

The patent of Siguel, entitled, "Method of diagnosis of fatty acid or lipid abnormalities," states in column 3, lines 55-65, that Mead acid is an essential fatty acid important in preventing essential fatty acid deficiency.

It would have been obvious for someone of ordinary skill in the art at the time of the instant invention to modify the lipid mixture analyses of Dionisi et al., Ruan et al., and Watkins et al. by the use of Mead acid in Siguel wherein the motivation would have been that Siguel shows the advantage of Mead acid in that adequate amounts of Mead acid are required to prevent lipid deficiency in the blood [see column 3, lines 55-65 of Siguel].

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Response to arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

The following rejection is newly applied:

Rejection #4 under 35 U.S.C. 103(a):

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dionisi et al. in view of Ruan et al. as applied to claims 2-3, 5-7, 15-16, and 56-58 above in further view of Dutta et al. [JAOCS, volume 74, no. 6, 1997, pages 647-657].

Claim 8 is further limiting the types of sterols to be employed as lipids.

Dionisi et al. and Ruan et al. make obvious a comparative profile of lipid concentrations, as discussed above.

Dionisi et al. and Ruan et al. do not teach use of cholestan-3b-ols.

The article of Dutta et al., entitled, "Studies of phytosterol oxides: I: Effect of storage on the content in potato chips prepared in different vegetable oils," states in the abstract:

Potato chips fried in palm oil, sunflower oil, and high-oleic sunflower oil were studied for the content of different phytosterol oxides during 0 to 25 weeks of storage in the dark. Oxidation products of sitosterol (2,4 alpha-ethyl-5-cholesten-2b-ol) and campesterol (2,4 alpha methyl-5cholesten-3b-ol) were synthesized to help identify the phytosterol oxides.

Dutta et al. continue in the introduction to explain in the first sentence of the introduction:

Abundant information exists on the formation of cholesterol oxidation products in foods and their biological implications, but there is relatively little on such products generated from phytosterols.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid quantification method of Dionisi et al. and Ruan et al. by use of the phytosterol quantitation method of Dutta et al. wherein the motivation would have been that the study of Dutta et al. has the advantage of using the required fatty acids for further understanding of biological implications of cholesterol and phytosterols (see introduction of Dutta et al. on page 647).

Response to arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

The following rejection is newly applied:

Rejection #5 under 35 U.S.C. 103(a):

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dionisi et al. in view of Ruan et al. above as applied to claims 2-3, 5-7, 15-16, and 56-58 above in further view of Grav et al. [Journal of Chromatography B, volume 658, 1994, pages 1-10].

Claim 10 is further limiting in the types of internal standards to be employed.

Dionisi et al. and Ruan et al. make obvious a comparative profile of lipid concentrations, as discussed above.

Dionisi et al. and Ruan et al. do not teach the specific internal standards to be used.

The article of Grav et al., entitled, "Gas chromatographic measurement of 3- and 4-thia fatty acids incorporated into various classes of rat liver lipids during feeding experiments," states in the first sentence of the abstract, "A practical procedure is described for the quantitative measurement of the amount of acyl units derived from tetradecylthioacetic acid (effecting hypolipemia in rats) and tetradecylthiopropionic acid (effecting hyperlipemia)."

The abstract of Grav et al. continues, "The overall recoveries of heptadecanoyl lipids added as internal standards using extraction were 94% to 96%, except for cholesteryl heptadecanoate..."

In Grav et al., section 2.3 on page 2, Grav et al. disclose that one of the species used in claim 10, diheptadecanoyl phosphatidylcholine is used as an internal standard.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid quantification method of Dionisi et al. and Ruan et al. by use of the use of the specific standards of Grav et al. wherein the motivation would have been that while Grav et al. disclose a method of quantifying lipids in livers, Grav et al. has the advantage of using the required internal standards in a direct health application in examining hypolipemia and hyperlipemia (see abstract of Grav et al.).

Response to arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

The following rejection is newly applied:

Rejection #6 under 35 U.S.C. 103(a):

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dionisi et al. in view of Ruan et al. above as applied to claims 2-3, 5-7, 15-16, and 56-58 above in further view of "The World of Membrane Lipids," [www.biochem.Missouri.edu/~lesa/LIPIDS/membrane_lipid.html; accessed on 6 December 2006, page made on 2 February 1999].

Claim 17 is further limiting wherein displaying generates a web page for viewing.

Dionisi et al. and Ruan et al. make obvious a comparative profile of lipid concentrations, as discussed above.

However, Dionisi et al. and Ruan et al. do not teach the use of a web page for electronically displaying of results.

"The World of Membrane Lipids," states in its introduction:

This website is an unofficial home for membrane lipid crystal structures. Here, you'll be able to find information about the nomenclature, crystallization, etc. of membrane lipids. Although about 50 structures are known, most of them are not in a database, so the only source of their coordinates is the original journal article. The purpose of this site is to make this information available to anyone interested, especially structural biologists. To facilitate their use, all coordinate files are in PDB format. If you have any comments or contributions, please send them to Lesa Beamer.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid quantification method of Dionisi et al. and Ruan et al. by use of the web posting database of "The World of Membrane Lipids," wherein the motivation would have been that posting lipid results on a web page has the advantage of making the data available to the general public (see introduction of "The World of Membrane Lipids").

Response to arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

The following rejection is newly applied:

Rejection #7 under 35 U.S.C. 103(a):

Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dionisi et al. in view of Ruan et al. above as applied to claims 2-3, 5-7, 15-16, and 56-58 above in further view of Seedorf et al. [Clinical Chemistry, 1995, volume 41, pages 548-552].

Claim 11 further limits the internal standards wherein the standard comprises stigmasterol for the lipid class of free sterols.

Claim 12 is further limiting wherein at least one of the quantitative lipid metabolite profiles is generated comprising separating a biological sample into fractions based on a plurality of lipid classes, wherein at least one quantitative internal standard is included for each lipid class; and measuring the quantity of a plurality of lipid metabolites in the fractions.

Dionisi et al. and Ruan et al. make obvious a comparative profile of lipid concentrations, as discussed above.

However, Dionisi et al. and Ruan et al. do not teach the required single internal standard for each of the lipids in the lipid class.

The article of Seedorf et al. studies the Smith-Lemli-Opitz syndrome diagnosed by using time of flight secondary ion mass spectrometry. The abstract of Seedorf et al. describes the use of stigmasterol as a standard by which to evaluate lipid class of free sterols.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the lipid quantification method of Dionisi et al. and Ruan et al. by use of the use of the specific standards of Seedorf et al. because it is obvious to combine known elements in the prior art to yield a predictable result. In this instance, the combination of Dionisi et al., Ruan et al., and Seedorf et al. yields an alternative method for assessing the composition of a lipomic mixture. There would have been a reasonable expectation of success for applying the use of internal standards for independent classes as in Seedorf et al. to the lipomic profiles of Dionisi et al. and Ruan et al. because using internal standards is a general means for accomplishing the analogous problem of analyzing the profile of a lipomic mixture.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61

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(November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)).

The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/
Russell S. Negin
23 November 2008

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631